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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,987	07/30/2001	David Nicholson Bell	6704-253	8386

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	8

DATE MAILED: 03/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,987	BELL ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-47 is/are pending in the application.

4a) Of the above claim(s) 32-47 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-31 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-47 are pending in the application.

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-33) in Paper No. 7 is acknowledged. Claims 34-47 are drawn to non-elected Groups and are withdrawn from consideration.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and 29 are drawn to methods for expanding TcR$\gamma\delta$+ T cells wherein the cells are cultured "in a first culture medium" comprising (a) a T cell mitogen (claims 1 and 29) or XLCM (claim 2), (b) interleukin-2 and (c) interleukin-4. The cells are then cultured "in a second culture medium comprising (i) interleukin-2 and (ii) interleukin-4". It is unclear if the first and second media are materially different (i.e. different chemical compositions) or if method comprises the application of a first culture medium followed by a second application of the same medium.

Claims 3-28 and 30-1 are dependent on claims 1, 2 or 3 and are therefore rejected for the same reason.

4. Claims 2 and 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the term "XLCM", which is the trade name of a culture medium. MPEP § 2173.05(u) states that if a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of the 35 U.S.C. 112, second paragraph. Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. In fact, the value of a trademark would be lost to the extent that it became descriptive of a product, rather than used as an identification of a source or origin of a product. Thus, the use of a trademark or trade name in a claim to identify or describe a material or product would not only render a claim indefinite, but would also constitute an improper use of the trademark or trade name.

Furthermore, the relationship between a trademark and the product it identifies is sometimes indefinite, uncertain, and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark. In patent specifications, every element or ingredient of the product should be set forth in positive, exact, intelligible language, so that there will be no uncertainty as to what is meant. Arbitrary trademarks which are liable to mean different things at the pleasure of manufacturers do not constitute such language. Ex Parte Kattwinkle, 12 USPQ 11 (Bd. App. 1931).

Claims 25-28 are dependent on claim 2 and are therefore rejected for the same reason.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5, 7-14, 16-23 and 25-28 are rejected under 35 U.S.C. 102(a) as being anticipated by Skea et al. (J. of Hematotherapy & Stem Cell Res., 8:525-538, 1999).

Skea et al. teaches a method for expansion of TcRγδ+ T cells where the cells are cultured in a fist culture medium comprising (a) a T cell mitogen (specifically XLCM), (b) interleukin-2 and (c) interleukin-4. Skea teaches that the medium XLCM and human sera or plasma was added to a final concentration of 5% (v/v) each, and the cells were passaged every 4-7 days into fresh medium (i.e. a second culture medium) (see p. 526, under XLCM and plasma preparation and T cell culture). Skea et al. also teach that ConA in the presence of IL-2 "provides the initial stimulus for the selective T cell expansion" (see p. 537, first paragraph). It is taught that the cells that are collected are peripheral blood LDMNC cells that are enriched by negative selection so that the cells are depleted of non- TcRγδ+ T cells including CD8+, CD14+ CD16+ CD19+, CD56+, glycophorin A+ and TcRαβ T cells (see p. 526 under T cell culture and Enrichment of T cell subsets).

7. Claims 1-5, 7-14, 16-23 and 25-28 rejected under 35 U.S.C. 102(a) as being anticipated by Skea et al. (Journal of Hematotherapy; 8:129-139, 1999).

Skea et al. teaches a method for expansion of TcRγδ+ T cells where the cells are cultured in a fist culture medium comprising (a) a T cell mitogen (specifically XLCM), (b) interleukin-2 and (c) interleukin-4. Skea teaches that the medium XLCM and human sera or plasma was added to a final concentration of 5% (v/v) each, and the cells were passaged every 4-7 days into fresh medium (i.e. a second culture medium) (see p. 130-131, under Culture Conditions). Skea et al. also teach that ConA is added to the medium at a concentration of 20μg/ml (see p. 130, under Preparation of XLCM™ and plasma). It is taught that the cells that are collected are peripheral blood LDMNC cells that are enriched for CD4+ and CD8+ T cells (see p. 131-132, under Enrichment of T cell subsets).

8. Claims 1-5 and 10-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Bell et al. (WO 98/33891, published 6 Aug. 1998).

Bell et al. teaches a method for expanding TcRγδ+ T cells in a starting sample comprising:

(1) culturing cells in the starting sample in a first culture medium comprising (a) a T cell mitogen, (b) interleukin-2 and (c) interleukin-4; and

(2) culturing the cells obtained in step (1) in a second culture medium comprising (i) interleukin-2 and (ii) interleukin-4 to expand TcRγδ+ T cells.

See, for example: Example 8, p. 32, which refers to the preparation of cells as described in Example 1D. Example 1D p. 20, lines 10-17 teaches that at every time point, the cells were

sub-cultured by diluting an appropriate volume of the cultured cells in fresh media containing 5% CM (note: 5% CM is deemed identical to 5% XLCM). This constitutes the use of a first and second culture media containing a T cell mitogen, IL-2 and IL-4 as it is taught that CM contains ConA, IL-2 and IL-4 (see p. 18 which describes the preparation and composition of CM). It is also taught that the T cell mitogen can be at a concentration of 1μg/ml (see p.22, line 22) or 20μg/ml (see p.18, line 1), IL-2 can be present at 0.6-15ng/ml (see p.22, Table 3) or at 12-159ng/ml (see page 18, Table 1), and IL-4 can be present at <0.008 (see p. 18, Table1) or 10ng/ml (see p. 22, Table 3).

Although Bell et al. does not specifically use the name XLCM, the CM prepared in Bell et al. appears to be the same as description of XLCM in the instant application (see p. 12, lines 6-10 of the specification and compare to Example 1 of Bell et al.). Therefore the CM used by Bell is deemed to be inherently the same as the XLCM used in claims 2 and 25-28 of the instant application.

Bell et al. does teach that the first and second media contain plasma at a concentration of 5% (see p. 22 and claim 12), that the starting cells are enriched for T cells and CD4+ cells (see p. 30, lines 7-16). Bell et al. also teaches that the sample is human peripheral blood cells the LDMNC fraction of human peripheral blood (see claim 1 and p. 14, lines 1-5).

9. Claims 1-5 and 9-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Bell et al. (U.S. Patent number 6,194,207 B1).

Bell et al. teaches a method for expanding TcRγδ+ T cells in a starting sample comprising:

(1) culturing cells in the starting sample in a first culture medium comprising (a) a T cell mitogen, (b) interleukin-2 and (c) interleukin-4; and

(2) culturing the cells obtained in step (1) in a second culture medium comprising (i) interleukin-2 and (ii) interleukin-4 to expand TcRγδ+ T cells.

See, for example: Example 7 (col. 19), which refers to the preparation of cells as described in Example 1C. Example 1C (col. 12) teaches that at every time point, the cells were sub-cultured by diluting an appropriate volume of the cultured cells in fresh media containing 0-10% CM (note: CM is deemed identical to XLCM). This constitutes the use of a first and second culture media containing a T cell mitogen, IL-2 and IL-4 as it is taught that CM contains ConA, IL-2 and IL-4 (see Examples 1A and 1B, col. 11-12; describing the preparation and composition of CM). It is also taught that the T cell mitogen can be at a concentration of 1μg/ml (see col. 14, line 39) or 20μg/ml (see col. 13, lines 42-43), IL-2 can be present at 0.6-15ng/ml (see col. 4, Table 3) or at 12-159ng/ml (see 12, Table 1), and IL-4 can be present at <0.008 (see col. 12, Table1) or 10ng/ml (see col. 14, Table 3).

Although Bell et al. does not specifically use the name XLCM, the CM prepared in Bell et al. appears to be the same as description of XLCM in the instant application (see p. 12, lines 6-10 of the specification and compare to Example 1 of Bell et al.). Therefore the CM used by Bell is deemed to be inherently the same as the XLCM used in claims 2 and 25-28 of the instant application.

Bell et al. does teach that the first and second media contain plasma at a concentration of 5% (see col. 13, line 42), that the starting cells are enriched for T cells and CD4+ cells (see

example 7, col. 19, lines 10-20). Bell et al. also teaches that the sample is human peripheral blood cells the LDMNC fraction of human peripheral blood (see col. 9, lines 12-19).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bell et al. (WO 98/33891) in view of Thomas et al. (U.S. Patent 5,877,299).

Bell et al. teaches a method for expanding TcR$\gamma\delta$+ T cells in a starting sample comprising:

(1) culturing cells in the starting sample in a first culture medium comprising (a) a T cell mitogen, (b) interleukin-2 and (c) interleukin-4; and

(2) culturing the cells obtained in step (1) in a second culture medium comprising (i) interleukin-2 and (ii) interleukin-4 to expand TcRγδ+ T cells.

See, for example: Example 8, p. 32, which refers to the preparation of cells as described in Example 1D. Example 1D p. 20, lines 10-17 teaches that at every time point, the cells were sub-cultured by diluting an appropriate volume of the cultured cells in fresh media containing 5% CM (note: 5% CM is considered identical to 5% XLCM). This constitutes the use of a first and second culture media containing a T cell mitogen, IL-2 and IL-4 as it is taught that CM contains ConA, IL-2 and IL-4 (see p. 18 which describes the preparation and composition of CM). It is also taught that the T cell mitogen can be at a concentration of 1μg/ml (see p.22, line 22) or 20μg/ml (see p.18, line 1), IL-2 can be present at 0.6-15ng/ml (see p.22, Table 3) or at 12-159ng/ml (see page 18, Table 1), and IL-4 can be present at <0.008 (see p. 18, Table1) or 10ng/ml (see p. 22, Table 3).

Although Bell et al. does not specifically use the name XLCM, the CM prepared in Bell et al. appears to be the same as description of XLCM in the instant application (see p. 12, lines 6-10 of the specification and compare to Example 1 of Bell et al.). Therefore the CM used by Bell is deemed to be the same as the XLCM used in claims 2 and 25-28.

Bell et al. does teach that the first and second media contain plasma at a concentration of 5% (see p. 22 and claim 12), that the starting cells are enriched for T cells and CD4+ cells (see p. 30, lines 7-16). Bell et al. also teaches that the sample is human peripheral blood cells the LDMNC fraction of human peripheral blood (see claim 1 and p. 14, lines 1-5).

Bell et al. does not explicitly teach that the starting cells are depleted of CD14+, CD16+, CD19+, CD56+, glycophorin A+ cells, TcRαβ+ T cells, and other non-TcRγδ+ T cells. Bell et al. also teaches the types of antigens (i.e. CD) expressed by different T cells (see p. 28, Table 8), and that, " when CD4+ enriched T cells were cultured in CM/P, the proportion of TcRγδ+ T cells was reproducibly increased."

Thomas et al. teaches a negative selection technique to remove CD14+, CD16+, CD19+, CD56+, glycophorin A+ cells, TcRαβ+ T cells, and other non-TcRγδ+ T cells (see col.3, lines 32-62; and Tables 2 and 3).

Therefore, it would have been prima facie obvious to one of ordinary skill in that art at the time of invention to combine the teachings of Bell et al. and Thompson et al. to devise a method of TcRαβ+ T cell expansion comprising removing CD14+, CD16+, CD19+, CD56+, glycophorin A+ cells, TcRαβ+ T cells, and other non-TcRγδ+ T cells from a starting sample of peripheral blood (using the method of Thompson et al.) in order to obtain a more purified sample of TcRγδ+ T cells.

The motivation to combine the references and create the method would have been to increase the efficacy of TcRγδ+ T cell expansion (using the expansion method of Bell et al.).

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

JEFFREY FREDMAN
PRIMARY EXAMINER

J. Eric Angell, Ph. D.
March 22, 2002